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NEWS 2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS 3	Feb 06	Engineering Information Encompass files have new names
NEWS 4	Feb 16	TOXLINE no longer being updated
NEWS 5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS 6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7	May 07	DGENE Reload
NEWS 8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS 9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI

NEWS EXPRESS	July 11 CURRENT WINDOWS VERSION IS V6.0b, CURRENT MACINTOSH VERSION IS V5.0C (ENG) AND V5.0JB (JP), AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2001
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=> s chimeric oligonucleotide?
L1          585 CHIMERIC OLIGONUCLEOTIDE?

=> s l1 and 5' and thymidine
MISMATCHED QUOTE 'AND 5' AND'
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> s l1 and thymidine
L2           11 L1 AND THYMIDINE

=> dup rem l2
DUPLICATE IS NOT AVAILABLE IN 'REGISTRY'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L2
L3            9 DUP REM L2 (2 DUPLICATES REMOVED)

=> d l3 ibib abs 1-
YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L3   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:167846  CAPLUS
DOCUMENT NUMBER:          134:217995
TITLE:                    Single-stranded oligodeoxynucleotide mutational
                          vectors for introduction of predetd. genetic changes
                          in target genes of a living cell
INVENTOR(S):              Metz, Richard A.; Frank, Bruce L.; Walther, Debra M.
PATENT ASSIGNEE(S):       Valigen (US), Inc., USA
SOURCE:                   PCT Int. Appl., 26 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
     WO 2001015740      A1   20010308      WO 2000-US23457   20000825
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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PRIORITY APPLN. INFO.: US 1999-384960 A 19990827

AB The present invention is based on the unexpected discovery that single-stranded oligodeoxynucleotides, particularly when appropriately modified or placed in a compn. with a suitable macromol. carrier, can be as or more effective in making predetd. genetic changes to target genes in cells as the prior art, i.e., Kmiec type mutational vectors. A single stranded oligodeoxynucleotide suitable for use according to the present invention is termed hereafter a Single-Stranded Oligodeoxynucleotide Mutational Vector or a SSOMV. The oligodeoxynucleotides are effective in animal, plant and bacterial cells. Specific end modifications that greatly increase the effectiveness of the oligodeoxynucleotides in bacteria are described. In preferred embodiments the oligodeoxynucleotide is modified by the attachment of 3' and 5' blocking substituents such as a 3'-3' linked cytosine nucleotide and a 5' linked indocarbocyanine dye. In an alternative embodiment the modification can consist of the replacement of the 3' most and/or 5' most internucleotide phosphodiester linkage with anon-hydrolyzeable linkage such as a phosphorothioatediester linkage or a phosphoramidate linkage. Surprisingly, unmodified oligodeoxynucleotides can be as effective in mammalian cells, including in vivo hepatocytes, as the modified nucleotides and can be as effective or more effective than **chimeric oligonucleotides** that consist of a mixt. of deoxynucleotides and 2'-O-Me ribonucleotides.

REFERENCE COUNT: 9

REFERENCE(S):

(1) Boussif; Proceedings of the National Academy of Sciences 1995, V92, P7297 CAPLUS
(2) Brush; US 5808044 A 1998 CAPLUS
(3) Campbell; The New Biologist 1989, V1(2), P223 CAPLUS
(4) Hunger-Bertling; Molecular and Cellular Biochemistry 1990, V92, P107 CAPLUS
(5) Kunzelmann; Gene Therapy 1996, V3, P859 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1

ACCESSION NUMBER: 1999:240162 CAPLUS

DOCUMENT NUMBER: 130:338340

TITLE: 2'-deoxyribo-PNAs: a structurally novel class of polyamide nucleic acids with good RNA and DNA binding affinity

AUTHOR(S): Von Matt, Peter; De Mesmaeker, Alain; Pieles, Uwe; Zurcher, Werner; Altmann, Karl-Heinz

CORPORATE SOURCE: Novartis Pharmaceuticals Inc., Summit, NJ, 07901, USA

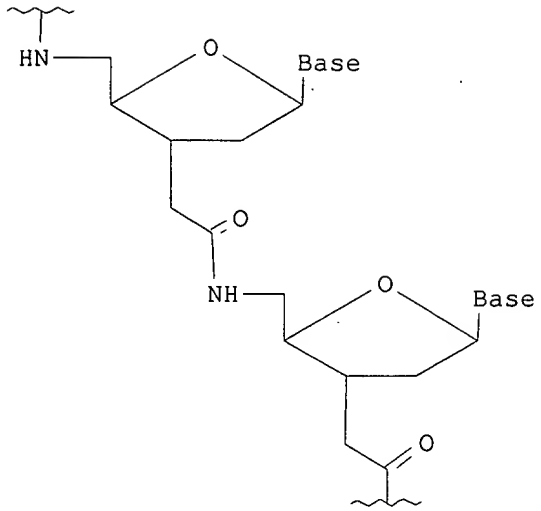
SOURCE: Tetrahedron Lett. (1999), 40(15), 2899-2902
CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB 2'-Deoxy-ribo polyamide nucleic acids (2'-deoxy-ribo-PNAs) (I) are a new class of DNA analogs with a 2',3'-dideoxy-ribose-polyamide backbone structure. 2'-Deoxy-ribo-PNAs as well as **chimeric oligonucleotide** analogs with a mixed DNA / 2'-deoxy-ribo-PNA structure bind to single stranded complementary nucleic acids with similar affinities as natural DNA.

REFERENCE COUNT: 31

REFERENCE(S):
(1) Altmann, K; Chimia 1996, V50, P168 CAPLUS
(3) Atherton, E; J Chem Soc, Chem Commun 1985, P165 CAPLUS
(4) Bannwarth, W; Helv Chim Acta 1988, V71, P1517 CAPLUS
(5) Crooke, S; Med Res Rev 1996, V16, P319 CAPLUS
(6) De Mesmaeker, A; Acc Chem Res 1995, V28, P366 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:184007 CAPLUS

DOCUMENT NUMBER: 128:240335

TITLE: Mammalian and human gene REC2 recombinases to induce transformation by homologous recombination and their promoters for sensitization of cells to irradiation

INVENTOR(S): Holloman, William K.; Rice, Michael C.; Smith, Sheryl T.; Shu, Zhigang; Kmiec, Eric B.

PATENT ASSIGNEE(S): Thomas Jefferson University, USA; Cornell Research Foundation, Inc.

SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9811214 A1 19980319 WO 1997-IB1217 19970911
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9743159 A1 19980402 AU 1997-43159 19970911
EP 961827 A1 19991208 EP 1997-941157 19970911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2001500729 T2 20010123 JP 1998-513444 19970911
PRIORITY APPLN. INFO.: US 1996-25929 P 19960911
WO 1997-IB1217 W 19970911

AB The invention concerns mammalian recombinase genes (REC2) and their promoters. Overexpression of gene REC2 recombinase in a cell is found to facilitate homologous recombination, particularly homologous recombination using a DNA/RNA **chimeric oligonucleotide** and to sensitize a cell to the apoptotic effects of irradn. The REC2 promoter, in combination with a strong enhancer, e.g., a SV40 enhancer, was found to be a strong promoter following irradn. of the cells. A radiation induceable promoter can be used to sensitize a cell to radiation treatment by operably linking the radiation-induceable promoter to a gene whose expression converts a prodrug to a drug such as a herpes **thymidine** kinase gene.

L3 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:667123 CAPLUS
DOCUMENT NUMBER: 130:14156
TITLE: Nucleoside 3'-O-(2-oxo-"spiro"-4.4-pentamethylene-1.3.2-oxathiaphospholane)s: monomers for stereocontrolled synthesis of oligo(nucleoside phosphorothioate/phosphate)s
AUTHOR(S): Karwowski, Boleslaw; Guga, Piotr; Kobylanska, Anna; Stec, Wojciech J.
CORPORATE SOURCE: Centre of Molecular and Macromolecular Studies, Department of Bioorganic Chemistry, Polish Academy of Sciences, Lodz, 90-363, Pol.
SOURCE: Nucleosides Nucleotides (1998), 17(9-11), 1747-1759
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Attempts at synthesis of **"chimeric" oligonucleotide** constructs (PO/PS-Oligos) possessing phosphate and P-stereo-defined phosphorothioate inter-nucleotide linkages via combined phosphoramidite/oxathiaphospholane methods were unsuccessful. Therefore, novel monomers for oxathiaphospholane method, namely 5'-O-DMT-deoxyribonucleoside 3'-O-(2-oxo-spiro-4.4-pentamethylene-1.3.2-oxathiaphospholane)s, were prepd. and used together with their diastereomerically pure 2-thio analogs for the stereocontrolled synthesis of **"chimeric" oligonucleotide** constructs (PO/PS-Oligos).

REFERENCE COUNT: 37
REFERENCE(S): (1) Alul, R; Nucleic Acids Res 1991, V19, P1527
CAPLUS

(3) Arnone, A; J Org Chem 1997, V62, P6401 CAPLUS
(4) Bryant, F; Biochemistry 1979, V18(13), P2825 CAPLUS
(5) Davis, F; Asymmetric Synthesis 1984, V4, P313 CAPLUS
(6) Drutsa, V; Dokl Akad Nauk SSSR 1977, V233, P595 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 9 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 2
ACCESSION NUMBER: 97357004 EMBASE
DOCUMENT NUMBER: 1997357004
TITLE: Synthesis and hybridization properties of modified oligonucleotides with PNA-DNA dimer blocks.
AUTHOR: Wenninger D.; Seliger H.
CORPORATE SOURCE: D. Wenninger, University of Ulm, Section of Polymers, Albert-Einstein-Allee 11, 89069 Ulm, Germany
SOURCE: Nucleosides and Nucleotides, (1997) 16/7-9 (977-980). Refs: 5
ISSN: 0732-8311 CODEN: NUNUD5
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Different modified PNA-DNA dimer-analogous synthons (I and II) were synthesized as phosphoramidites. These dimer units were assembled by a 5'-
modified deoxythymidine and a modified PNA monomer. These synthons were used in the routine coupling procedure for oligonucleotides. Therefore no PNA coupling chemistry is necessary to synthesize PNA-DNA **chimeric oligonucleotides**. Various deoxyoligonucleotides were synthesized introducing the dimer blocks I and II at different positions in the sequences. Melting temperatures of the modified oligonucleotides with their complementary DNA analogues were determined.

L3 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:969424 CAPLUS
DOCUMENT NUMBER: 124:146761
TITLE: Backbone-modified oligonucleotide analogs and solid phase synthesis
INVENTOR(S): Cock, Phillip Dan; Sanghvi, Yogesh S.; Morvan, Francois
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 72
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9518136	A1	19950706	WO 1994-US14883	19941228
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5541307	A	19960730	US 1993-174379	19931228
EP 737201	A1	19961016	EP 1995-906115	19941228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

US 6232463	B1	20010515	US 1998-128508	19980804
US 6146829	A	20001114	US 1998-144611	19980831

PRIORITY APPLN. INFO.:

US 1993-174379	A	19931228
US 1990-558663	A2	19900727
US 1990-566836	A2	19900813
US 1991-703619	A2	19910521
US 1992-903160	B2	19920624
US 1993-40903	A2	19930331
WO 1994-US14883	W	19941228
US 1997-861306	A3	19970421
US 1997-948151	A1	19971009

AB Compds. and methods for prepg. nuclease-resistant oligonucleotide analogs are provided. In preferred embodiments, the methods involve solid-phase coupling of synthons bearing either 3'-electrophilic groups and 5'-nucleophilic groups or 5'-electrophilic groups and 3'-nucleophilic groups to form neutral, achiral oligomers. In particular, amine-terminated synthons are coupled with aldehyde-terminated synthons to produce hydroxylamino- and/or hydrazino-contg. covalent linkages. Examples illustrate prepn. of a variety of nucleotide analogs, various nucleotide dimer and tetramer analogs contg. the novel linkages, and oligonucleotide analogs contg. both the novel and std. linkages. For instance, coupling of 5'-O-amino-N4-benzoyl-3'-O-tert-butyldiphenylsilyl-5-methyl-2'-deoxycytidine with 5'-O-tert-butyldiphenylsilyl-3'-deoxy-3'-C-formylthymidine to give an oxime, followed by deprotection of the benzamide function with NH3/MeOH, redn. of the oxime function with NaBH3CN, and reductive N-methylation with formaldehyde and NaBH3CN, gave the dimer TBDPS-O-T*MeC-O-TBDPS [TBDPS = tert-butyldiphenylsilyl; * = 3'-CH2NMeO-5' (hereafter "MMI") linkage; Me = 5-methyl] in 84% yield. This dimer was subjected to N-benzoylation, desilylation, tritylation, and phosphitylation, to give the dimer DMT-O-T*MeCBz-O-Amidite [DMT = 4,4'-dimethoxytrityl; Amidite = P(NPr-iso2)OCH2CH2CN; Bz = N4-benzoyl]. This and similar MMI-linkage dimers and tetramers were used to prep. **chimeric oligonucleotides** such as T*TPSC*TPSCPSGPSCPSTPSGPSGPSTPSGPSAPSGPST*TPST*C (code no. 9495; I; PS = phosphorothioate linkage). As an antisense oligonucleotide for PKC-.alpha. mRNA in A549 cells, I showed greater activity (IC50 = 80 nM) than the analogous std. oligonucleotide sequence with pure phosphorothioate linkages (IC50 = 175 nM).

L3 ANSWER 7 OF 9 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER:	96018268 EMBASE
DOCUMENT NUMBER:	1996018268
TITLE:	Oligonucleotides containing acyclic nucleoside analogues with carbamate internucleoside linkages.
AUTHOR:	Habus I.; Agrawal S.
CORPORATE SOURCE:	Hybridon Inc., One Innovation Drive,Worcester, MA 01605, United States
SOURCE:	Nucleosides and Nucleotides, (1995) 14/9-10 (1853-1859). ISSN: 0732-8311 CODEN: NUNUD5
COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article
FILE SEGMENT:	006 Internal Medicine 037 Drug Literature Index
LANGUAGE:	English
SUMMARY LANGUAGE:	English

AB Synthesis of 2'-deoxy-2',3'-secothymidine t and its dimer t*t, where the two 2'-deoxy-2',3'-secothymidine t units are connected via a carbamate,

*=3'-NH-CO-O-5', internucleoside linkage has been achieved. These building blocks were protected in the 5'-position, converted into their phosphoramidites, or attached onto CPG, and then used for '**chimeric oligonucleotide**' synthesis.

L3 ANSWER 8 OF 9 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95228197 EMBASE
DOCUMENT NUMBER: 1995228197
TITLE: The prooligonucleotide approach: II. Synthesis and stability studies of **chimeric oligonucleotide** models.
AUTHOR: Barber I.; Tosquellas G.; Morvan F.; Rayner B.; Imbach J.-L.
CORPORATE SOURCE: Laboratoire de Chimie Bio-Organique, URA 488 du CNRS, Universite de Montpellier II, Place Eugene-Bataillon,34095 Montpellier Cedex 5, France
SOURCE: Bioorganic and Medicinal Chemistry Letters, (1995) 5/14 (1441-1444).
ISSN: 0960-894X CODEN: BMCLE8
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Alkylation of a central gap of three phosphorothioate linkages into a dodecathymidine methylphosphonate with different iodoalkyl acylates yielded the corresponding neutral oligonucleotides. Upon incubation of these prooligonucleotides in cell extracts, the bioreversible alkyl acylate masking groups were selectively removed by carboxyesterases present in the milieu.

L3 ANSWER 9 OF 9 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 95:275925 SCISEARCH
THE GENUINE ARTICLE: QT138
TITLE: SITE-DIRECTED CLEAVAGE OF SINGLE INTERNUCLEOTIDE BONDS IN RIBOSOMAL-RNA
AUTHOR: BOGDANOVA S L; DEGTYAREV A I; BARANOV P V; DOKUDOVSKAYA S S; LAVRIK I N; DONTSOVA O A (Reprint); ORETSKAYA T S; KRYNETSKAYA N F; SHABAROVA Z A; BOGDANOV A A
CORPORATE SOURCE: MOSCOW MV LOMONOSOV STATE UNIV, SCH CHEM, MOSCOW 119899, RUSSIA (Reprint); MOSCOW MV LOMONOSOV STATE UNIV, SCH CHEM, MOSCOW 119899, RUSSIA
COUNTRY OF AUTHOR: RUSSIA
SOURCE: BIOCHEMISTRY-MOSCOW, (FEB 1995) Vol. 60, No. 2, pp. 217-224.
ISSN: 0006-2979.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 18
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The cleavage of 16S ribosomal RNA (rRNA) from E. coli with ''hammerhead'' ribozymes and with RNase H in the presence of ''chimeric'' (2'-deoxy-F-**thymidine** containing) oligonucleotides has been studied. The conditions for the cleavage of a desired single internucleotide bond in these large molecules with very complicated secondary and tertiary structures have been found.

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=> d history

     (FILE 'HOME' ENTERED AT 14:54:09 ON 19 JUL 2001)

     FILE 'MEDLINE, EMBASE, CAPLUS, SCISEARCH, BIOSIS, REGISTRY' ENTERED AT
     14:54:32 ON 19 JUL 2001
L1           585 S CHIMERIC OLIGONUCLEOTIDE?
L2            11 S L1 AND THYMIDINE
L3             9 DUP REM L2 (2 DUPLICATES REMOVED)

=> s l1 and blocking and group
L4             2 L1 AND BLOCKING AND GROUP

=> dup rem l4
DUPLICATE IS NOT AVAILABLE IN 'REGISTRY'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L4
L5             2 DUP REM L4 (0 DUPLICATES REMOVED)

=> s l1 and nuclease and protection
L6            10 L1 AND NUCLEASE AND PROTECTION

=> s l1 and nuclease and protect?
L7            14 L1 AND NUCLEASE AND PROTECT?

=> dup rem l7
DUPLICATE IS NOT AVAILABLE IN 'REGISTRY'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L7
L8             3 DUP REM L7 (11 DUPLICATES REMOVED)

=> d l8 ibib abs 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L8   ANSWER 1 OF 3     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:    97448861     MEDLINE
DOCUMENT NUMBER:     97448861   PubMed ID: 9303186
TITLE:               Studies on the mechanism of stabilization of partially
                     phosphorothioated oligonucleotides against nucleolytic
                     degradation.
AUTHOR:              Uhlmann E; Ryte A; Peyman A
CORPORATE SOURCE:    Lombardi Cancer Center, Georgetown University Medical
                     Center, Washington, DC 20007-2197, USA.
SOURCE:              ANTISENSE AND NUCLEIC ACID DRUG DEVELOPMENT, (1997 Aug) 7
                     (4) 345-50.
                     Journal code: CJY; 9606142. ISSN: 1087-2906.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199802
ENTRY DATE:          Entered STN: 19980217
                     Last Updated on STN: 19980217
                     Entered Medline: 19980205
AB   The use of chimeric oligonucleotides (ODN), in which
     certain phosphodiester internucleoside linkages are replaced by
     phosphorothioate (PS) linkages to provide protection against
     degradation by nucleases, is gaining increasing attention
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because of their significantly decreased propensity for nonantisense effects as compared with uniformly PS-modified ODN. We have recently reported that partially PS-modified ODN, in which end- capping is used to prevent hydrolysis by exonucleases in combination with PS **protection** at internal pyrimidine residues which are the major sites of endonuclease degradation, are surprisingly stable in serum. The present study investigates an additional role of the backbone modification in the stabilization of ODN against nucleolytic degradation. We show that the stability of an unmodified ODN in fetal bovine serum is significantly enhanced in the presence of PS-modified ODN. The magnitude of stabilization is strongly dependent on the type and degree of backbone modification. The observed effect is stronger for PS-modified ODN than for methylphosphonate (MP)-modified ODN and increases as the number of PS linkages in the ODN increases. Thus, **nuclease** stability of partially PS-modified ODN is not only caused by direct prevention of **nuclease** attack at the phosphate center but is additionally supported by interference of the **nucleases** with the PS groups of ODN, resulting in decreased degradation. As the degree of many nonantisense effects caused by ODN, such as protein interactions and B cell stimulation, is dependent on the backbone modification, our results may have implications for the use of non-ODN **nuclease** inhibitors to reduce undesirable side effects.

L8 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 96226169 MEDLINE
DOCUMENT NUMBER: 96226169 PubMed ID: 8657564
TITLE: Oligodeoxynucleoside phosphoramidates (P-NH2): synthesis and thermal stability of duplexes with DNA and RNA targets.
AUTHOR: Peyrottes S; Vasseur J J; Imbach J L; Rayner B
CORPORATE SOURCE: Laboratoire de Chimie Bio-Organique, Universite Montpellier II, Montpellier, France.
SOURCE: NUCLEIC ACIDS RESEARCH, (1996 May 15) 24 (10) 1841-8. Journal code: O8L; 0411011. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960808 Last Updated on STN: 19960808 Entered Medline: 19960731

AB Syntheses of non ionic oligodeoxynucleoside phosphoramidates (P-NH2) and mixed phosphoramidate- phosphodiester oligomers were accomplished on automated solid supported DNA synthesizer using both H-phosphonate and phosphoramidite chemistries, in combination with t-butylphenoxyacetyl for N-**protection** of nucleoside bases, an oxalyl anchored solid support and a final treatment with methanolic ammonia. Thermal stabilities of the hybrids formed between these new analogues and their DNA and RNA complementary strands were determined and compared with those of the corresponding unmodified oligonucleotides, as well as of the phosphorothioate and methylphosphonate derivatives. Dodecathymidines containing P-NH2 links form less stable duplexes with DNA targets, d(C2A12C2) (deltaTm/modification -1.4 degrees C) and poly dA (deltaTm/modification -1.1 degrees C) than the corresponding phosphodiester and methylphosphonate analogues, but the hybrids are

slightly more stable than the one obtained with phosphorothioate derivative. The destabilization is more pronounced with poly rA as the target (deltaTm/modification -3 degrees C) and could be compared with that found with the dodecathymidine methylphosphonate. The modification is less destabilizing in an heteropolymer-RNA duplex (deltaTm/modification -2 degrees C). As expected, the P-NH2 modifications are highly resistant towards the action of various **nucleases**. It is also demonstrated that an all P-NH2 oligothymidine does not elicit Escherichia coli RNase H hydrolysis of the poly rA target but that the modification may be exploited in **chimeric oligonucleotides** combining P-NH2 . sections with a central phosphodiester section.

L8 ANSWER 3 OF 3 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 3
ACCESSION NUMBER: 94121230 EMBASE
DOCUMENT NUMBER: 1994121230
TITLE: Synthesis of di-, tri-, and tetrameric building blocks with novel carbamate internucleoside linkages and their incorporation into oligonucleotides.
AUTHOR: Habus I.; Temsamani J.; Agrawal S.
CORPORATE SOURCE: Hybridon, Inc., One Innovation Drive,Worcester, MA 01605, United States
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SUMMARY LANGUAGE: English
AB Synthesis of di-, T*T, tri-, T*T*T, and tetrameric, T*T*T*T, building blocks with carbamate internucleoside linkage, * = 3'-NH-CO-O-5', was achieved by the reaction of mono-, di-, or trimeric nucleoside 5'-O-p-nitrophenyl carbonate intermediates with 30-amino-3'-deoxythymidine. These building blocks were suitably **protected** at 5'-position and converted into phosphoramidites, or attached onto CPG, and then used for the **'chimeric oligonucleotide'** synthesis. The novel oligonucleotides derived therefrom have been studied for their binding properties to complementary nucleic acids and for their **nuclease** sensitivity. Oligonucleotides containing one, two, or three carbamate linkages at 3'-end, were found to have increased **nuclease** resistance and did not effect the duplex stability significantly.

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